

## Operating under pressure: Is there a place for preoperative TIPS?



Cirrhosis as a comorbidity is responsible for almost half of cirrhosis-related hospitalisations, while the burden of liver disease has been steadily increasing, particularly in the Western world, largely due to metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol-related liver disease.<sup>1</sup> With improved long-term survival for patients with cirrhosis, surgery is becoming more common in this vulnerable patient population.<sup>2</sup> Portal hypertension (PHT) is the major driver of acute decompensation (AD), acute-on-chronic liver failure (ACLF) and mortality for patients with cirrhosis, especially in the context of surgery.<sup>3</sup>

This prompts the question of whether measures to lower PHT, such as transjugular intrahepatic portosystemic shunt (TIPS), can reduce the risk of postoperative complications and mortality. In a recent paper published in *JHEP Reports*, Piecha *et al.* address this question through a retrospective study comparing in-hospital mortality after surgery among 64 patients with cirrhosis who had received TIPS within 3 months of surgery to 131 patients with cirrhosis without prior TIPS.<sup>4</sup> Despite its major limitation of the retrospective design with an unmatched non-TIPS control group, the study reveals a striking reduction in in-hospital mortality for patients with TIPS compared to those without (19% vs. 40%). Furthermore, not only did patients with TIPS experience lower in-hospital mortality, but they also had fewer postoperative complications, including reduced need for blood transfusions and renal replacement therapy, as well as shorter stays in the intensive care unit. The incidence of AD with bleeding and hepatic encephalopathy (HE) was also lower in patients with preoperative TIPS (16% vs. 40% and 22% vs. 33%, respectively). Although the lower rates of HE may seem surprising at first, it is conceivable that the use of modern, controlled expansion TIPS stents, along with personalized tailoring of stent diameter size, contribute to lower rates of HE or, at the very least, prevent them from increasing compared to similar patients without TIPS.<sup>5,6</sup> This suggests that whilst PHT is addressed by TIPS, the pathophysiological trigger for AD (and particularly HE) might be the surgical trauma itself, with some evidence from animal models of cirrhosis showing that visceral manipulation alone can further elevate portal pressure.<sup>7</sup>

While the study by Piecha *et al.* provides valuable insights into the potential benefits of preoperative TIPS on mortality, it raises two major questions: 1) Why does TIPS improve postoperative outcomes? 2) What are the specific patient selection criteria?

To address the first question, a closer look into the causes of postoperative deaths is required. In a well-characterized, large retrospective cohort of patients with cirrhosis, Klein and Chang *et al.* showed that one in three patients with cirrhosis undergoing surgery develops postoperative ACLF, and 40% of them died.<sup>8</sup> Another study by Chang *et al.* demonstrated that surgical site infections (occurring in any part of the body deeper than the fascial/muscle layers manipulated during the procedure)

precipitate ACLF and more than double its risk.<sup>9</sup> Yet, adequate empiric antibiotic therapy improved 6-month survival. These findings are supported by the PREDICT study, which identified bacterial infections as the main precipitants of ACLF development in hospitalized patients with cirrhosis.<sup>10</sup> Indeed, it was recently shown that preoperative TIPS significantly lowers the risk of postoperative ACLF development within 90 days (13% vs. 33%),<sup>11</sup> which translates into lower mortality (18% vs. 38%), results that are echoed in the study by Piecha *et al.* In both studies, rates of postoperative hepatic AD (ascites, bleeding) were also lower in the group of patients with preoperative TIPS. It appears that the presence of TIPS in patients with cirrhosis before surgical procedures leads to lower rates of AD, thus raising the threshold for postoperative ACLF development and death.

The second question regarding patient selection hinges on risk stratification. One of the more recent risk stratification models, derived from a US Veterans Affairs cohort of 3,785 patients, is known as the VOCAL-Penn cirrhosis surgical risk score and has shown good predictive ability in two American validation cohorts.<sup>12,13</sup> This score includes various factors such as age, albumin, bilirubin, platelets, obesity, NAFLD (non-alcoholic fatty liver disease), ASA score, as well as the type and urgency of surgery. PHT is indirectly reflected through the platelet count. Interestingly, in the current study by Piecha *et al.*, VOCAL-Penn underestimates mortality in patients without preoperative TIPS, whereas in the study by Chang *et al.*, its performance at 90 days was fair (AUC 0.70).<sup>4,9</sup> This suggests a regional bias (America and Europe) and an underrepresentation of PHT (or its treatment) in the model. Consequently, we need additional methods to identify patients who would benefit from preoperative TIPS. Indeed, we obtain more granular data from these studies. Piecha *et al.* reported that preoperative TIPS was associated with the most significant survival benefit vs. no TIPS in patients with Child-Pugh class B and C cirrhosis (11% vs. 46% and 33% vs. 78%, respectively). There was no significant benefit in patients with Child-Pugh class A cirrhosis. Similarly, Chang *et al.* previously demonstrated that the greatest benefit of preoperative TIPS in preventing postoperative ACLF occurred in patients with a CLIF-C AD score >45 points. The results of these two independent studies transmit a similar message to a study on the use of preemptive TIPS for acute variceal bleeding, where TIPS significantly improves survival in patients with Child-Pugh class B >7 (and active bleeding in endoscopy) or Child-Pugh class C <14 cirrhosis.<sup>14</sup> Interestingly, the “window of opportunity” for TIPS placement in the context of surgery seems to open for patients with Child-Pugh class B/C and/or a CLIF-C AD score >45 points. Nevertheless, caution is advised, as only 22% of patients received TIPS specifically for surgery without a PHT-related indication in the study by Piecha *et al.*, while almost half of the patients received TIPS for refractory ascites (38%) or acute variceal bleeding (9%).<sup>4</sup> Moreover, 52% of patients showed ascites at the time of surgery, suggesting that some patients may have experienced either TIPS dysfunction or an inadequate clinical response

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to TIPS. This heterogeneity in the risk and trajectory of ACLF development makes it challenging to draw definitive conclusions.

Besides treatment of PHT, there are initiatives specifically to improve the outcomes of surgical procedures, such as the implementation of enhanced recovery after surgery (ERAS) programmes, which have focused on optimizing perioperative care in recent years.<sup>15</sup> However, current ERAS guidelines are not specifically tailored to patients with cirrhosis.

Where does this leave us? Do we need to include TIPS in ERAS, or should we continue to operate under (high portal

pressure? We now have data suggesting that strategies to reduce portal pressure through TIPS before surgery can mitigate the risk of ACLF and mortality, although further validation is required. Meticulous patient selection is also paramount for the clinical success of TIPS, and more refined selection criteria are needed before recommendations for routine preoperative TIPS can be made. For the time being, TIPS should be considered early in cases of AD and when elective surgery is deemed necessary in patients with cirrhosis, always taking into account risk-benefit considerations on a case-by-case basis.

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### Conflict of interest

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### Authors' contributions

MP, JT: Concept and design, drafting of the manuscript, critical revision of the manuscript for important intellectual content.

### Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhepr.2024.101034>.

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